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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/758,036	Applicant(s) Leberer et al.
	Examiner William Sandals	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 1, 2002*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above, claim(s) *11-18 and 22-24* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-10 and 19-21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Nov 1, 2002* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. The amendments to claims 1, 3-9 and 19-21 submitted in Paper No. 15, submitted on November 1, 2002 have been entered. Claims 1-24 are pending. Claims 11-18 and 22-24 drawn to a non-elected invention have been withdrawn.

2. Amendments to the specification in Paper No. 15 have overcome the objections to the specification, and the objections are withdrawn.

3. Amendments to the claims in Paper No. 15 have overcome the objections to the claims, and the objections are withdrawn.

4. Amendments to the claims in Paper No. 15 have overcome the rejections of the claims under 35 USC 112, second paragraph, and the rejections are withdrawn.

5. Arguments filed in Paper No. 15 regarding the rejection of the claims under 35 USC 103(a) have been fully considered but they are not persuasive. The response to the arguments is contained in the rejection repeated below.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

Drawings

7. The drawings as submitted on November 1, 2002, have been approved by the draftsman.

Claim Objections

8. Claim 19 is objected to because of the following informalities: Claim 19 depends from claim 17. Claim 17 is drawn to a non-elected invention and is therefore withdrawn from examination. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 4 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 4 recites that gpIRK1 is a human potassium channel. "gp" stands for guinea pig. The gpIRK1 potassium channel of claim 4 is isolated from guinea pig heart muscle. The gpIRK1 potassium channel of claim 4 is therefore not a human potassium channel. This inconsistency in the claimed subject matter renders the meaning of the claim vague and indefinite.

12. Claim 19 provides for the use of the mutated S. cerevisiae cell of claim 17, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 19 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-3 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,795,770 (Gaber) in view of Ketchum et al. and Fairman et al.

The claims are drawn to a process for identifying inhibitors or activators of a eukaryotic potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1 and wherein a eukaryotic heterologous potassium channel is expressed in the mutant cell. The inhibitor or activator is added to the mutant cells and the effect of the inhibitor or activator is determined. A substance may be added in addition to an activator to determine the effect of the substance on the cells in the presence of the activator.

Gaber taught at the abstract, column 1, lines 37-50 and bridging from line 66 to column 2, line 21, column 3, lines 37-67 and column 8, lines 23-27 a process for identifying inhibitors or activators of a eukaryotic potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1 or TRK1 and TRK2. A eukaryotic heterologous potassium channel is expressed in the mutant cell. The inhibitor or activator is added to the mutant cells and the effect of the inhibitor or activator is determined. A substance may be added in addition to an activator to determine the effect of the substance on the cells in the presence of the activator. Gaber taught that the beneficial and desirable feature of the mutant *S. cerevisiae* cells was their inability to transport potassium into *S. cerevisiae* cells to facilitate the discovery of heterologous eukaryotic potassium channels, and to test for inhibitors and activators of potassium channels.

US 5,795,770 did not teach that the mutant *S. cerevisiae* cells were inactivated for TOK1.

Ketchum et al. taught (see especially page 692, column 2) that *S. cerevisiae* cells contained a potassium channel TOK1 which transported potassium out of *S. cerevisiae* cells, and that under certain conditions, also transported potassium into *S. cerevisiae* cells.

Fairman et al. taught at the abstract, page 150, column 1, the last 20 lines of the introduction, materials and methods section "plasmids and strains", page 152 columns 1 and 2, page 153 bridging to page 154 - "deletion of TOK1", page 154, "Discussion" - first paragraph, page 155 - "K+ influx..." and page 155 "the possible physiological role of K+ influx through

TOK1" bridging to page 156, that *S. cerevisiae* cells contained a potassium channel, TOK1, which transported potassium out of *S. cerevisiae* cells, and that under certain conditions, also transported potassium into *S. cerevisiae* cells. Fairman et al. taught mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1 designated delta TRK1, delta TRK2, delta TOK1. Fairman et al. report at page 153, column 2 bottom, bridging to the top of page 154, column 1 top that the triple mutant grew poorly on potassium limiting media.

It would have been prima facie obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Gaber with Ketchum et al. and Fairman et al. to produce the instant claimed invention because each of Gaber, Ketchum et al. and Fairman et al. taught mutant *S. cerevisiae* cells with inactivated endogenous potassium uptake channels used in methods of evaluation of the effects on cells which were deficient in potassium uptake. Fairman et al. make obvious the use of a TRK1, TRK1, TOK1 deficient mutant which was useful in a method of evaluation of the effects on cells which were deficient in potassium uptake.

One of ordinary skill in the art would have been motivated to combine the teachings of Gaber with Ketchum et al. and Fairman et al. to produce the instant claimed invention because both Fairman et al. and Ketchum et al. taught that TOK1 was a potassium transport channel which was capable of transporting potassium into cells. Further, Fairman et al. teach that the mutant cell with inactivated endogenous potassium channels TRK1, TRK2 and TOK1 grew very

poorly on potassium limiting media. Therefore, given that TOK1 is a potassium uptake transporter, one of skill in the art would be motivated to delete TOK1 to produce mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1 to practice the method of identifying activators and inhibitors of heterologous potassium channel uptake transporters expressed in mutant *S. cerevisiae* cells as taught by Gaber. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US 5,795,770 with Ketchum et al. and Fairman et al.

15. Claims 1-10 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ketchum et al. and Fairman et al. as applied to claims 1-3 and 19-21 above, and further in view of Tang et al. and Rampe et al.

The claims are drawn to the invention as described above and where the human potassium channel is HERG1, Kv1.5 or gpIRK1, and expression is detected by a growth reporter.

Ketchum et al. and Fairman et al. teach the invention as described above.

Ketchum et al. and Fairman et al. did not teach that the human potassium channel is HERG1, Kv1.5 or gpIRK1, and expression is detected by a growth reporter.

Tang et al. teach at the abstract, page 1232, column 1, middle paragraph, and at the figures, the expression of gpIRK1 potassium channel in saccharomyces TRK1, TRK2 double

deletion mutant to study the effect of gpIRK1 potassium channel on cell growth and potassium transport in the saccharomyces double mutant with a growth reporter. Tang et al. studied the effects of inhibitors on the growth of the double mutant which expressed the gpIRK1 potassium channel. gpIRK1 is a potassium channel from guinea pig heart muscle. The gpIRK1 is also expressed in oocytes for studying the effects of the potassium channel. Tang et al. teach that it is desirable and useful to study heart muscle potassium channels to understand their critical importance in heart action.

Rampe et al. teach at the abstract, introduction and the figures the human potassium channels Kv1.5 and HERG. These potassium channels are from heart muscle. Rampe et al. teach that it is desirable and useful to study the action of heart muscle potassium channels, and to study the action of inhibitors and activators of heart muscle potassium channels.

It would have been prima facie obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Gaber, Ketchum et al., Fairman et al., Tang et al. and Rampe et al. to produce the instant claimed invention because each of Gaber, Ketchum et al., Fairman et al., Tang et al. and Rampe et al. teach the studying of potassium uptake channels used in methods of evaluation of the effects on cells deficient in expressing normal potassium channels. Tang et al. make obvious the use of a TRK1, TRK2 deficient mutant which was useful in a method of evaluation of heart muscle potassium channels on cells which were deficient in potassium uptake. Rampe et al. make obvious the use of human heart muscle cell potassium channels expressed in cells which are deficient in potassium uptake to test

the affect of activators and inhibitors of potassium uptake on the human heart muscle potassium channels HERG and Kv1.5.

One of ordinary skill in the art would have been motivated to combine the teachings of Gaber, Ketchum et al., Fairman et al., Tang et al. and Rampe et al. to produce the instant claimed invention because Tang et al. teach the desirability of expressing heart muscle potassium channels in *S. cerevisiae* cells which are deficient in TRK1 and TRK2 potassium channels to study the effects of the heart muscle potassium channels in these deficient cells, as taught by Gaber, Ketchum et al. and Fairman et al. Rampe et al. teach the desirability to study the effects of activators and inhibitors of heart muscle potassium channels in cells which have deficient endogenous potassium channels as taught by Gaber. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Gaber, Ketchum et al., Fairman et al., Tang et al. and Rampe et al.

Response to Arguments

16. Arguments set forth in Paper No. 15, page 8, assert that Gaber was filed in 1997, and that Ketchum et al. was published in 1995, therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Ketchum et al. with Gaber. But, since Gaber did not mention Ketchum et al. it was therefore not obvious to combine the references.

This argument is not entirely correct, since the Gaber reference is a US patent with an actual filing date of April 27, 1992. The teachings of Gaber therefore occurred prior to the

teachings of Ketchum et al. Further, the argument also does not exclude the possibility that an ordinary skilled artisan may or may not choose to observe the teachings of another, despite obvious teachings in the prior art as cited above.

17. Arguments set forth in Paper No. 15, page 8, assert that Gaber teaches away from the instant claimed invention by pointing to Gaber at column 3, lines 41-50 where it states that mutants in TRK1 and TRK2 may not be necessary to study the effects of potassium uptake on cell growth of *S. cerevisiae*.

At column 3, lines 38-41 it states "[i]n the present invention, the endogenous TRK1 (or TRK! and TRK2) transporters are deleted in order to 1) detect function of the heterologous in channel and 2) to make the strain dependent on the heterologous channel for growth." This makes clear the inclusion of deletion mutants for endogenous potassium channels as contemplated for the practice of the invention as taught by Gaber.

18. Arguments set forth in Paper No. 15, page 8, assert that the obviousness statement of this rejection is "conclusory" and does not have proper support to make the assertion of obviousness.

As stated in the above rejection, the obviousness is prima facie obvious. The motivation is correct since the motivation statement is directed to the teachings of the references which clearly motivate one of ordinary skill in the art to practice the study of expression of heterologous potassium channels from eukaryotes (humans) in cells which are deficient in endogenous expression of potassium channels.

19. Arguments set forth in Paper No. 15, page 9, assert that Fairman et al. teach that despite the knockout of TRK1, TRK2 and TOK1, *S. cerevisiae* cells were still able to grow, and therefore, the knockout of these three genes would not ensure a reasonable expectation of success. Thus, one of ordinary skill in the art would not be motivated to use the cells of Fairman et al. in combination with Gaber.

The teachings of Fairman et al. demonstrate that the triple knockout of TRK1, TRK2, TOK1 is significantly more growth inhibited than the double knockout of TRK1, TRK2. This makes the triple knockout cells of Fairman et al. more desirable than the double knockout cells of Fairman et al. and Gaber. In addition, the instant claimed invention uses these same cells with success. There does not appear to be any distinction between the triple knockout cells of Fairman et al. and the instant claimed triple knockout cells. Therefore, one of ordinary skill in the art would have a reasonable expectation of success using the same triple knockout cells to produce the instant claimed invention by combination of Fairman et al. and Gaber.

20. Arguments set forth in Paper No. 15, page 9, assert that the oocyte cells of Ketchum are different from the *S. cerevisiae* cells of Gaber, and one of ordinary skill in the art would not be motivated to combine the teachings based upon oocyte with teachings based upon *S. cerevisiae* cells.

The teachings of Tang et al. use both the double knockout *S. cerevisiae* cells and oocytes to demonstrate the usefulness of studying expression of heterologous potassium channels in cells

deficient in endogenous expression of potassium channels. This makes the combination prima facie obvious to one of ordinary skill in the art at the time of filing the instant application.

Conclusion

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.
Examiner

January 26, 2003

JAMES KETTER
PRIMARY EXAMINER